```
=> d his ful

     (FILE 'HOME' ENTERED AT 14:07:00 ON 14 NOV 2005)

     FILE 'HCAPLUS' ENTERED AT 14:12:08 ON 14 NOV 2005
L1           125 SEA ABB=ON  PLU=ON  "RODRIGUEZ MOSES"/AU
L2           154 SEA ABB=ON  PLU=ON  "PEASE L"/AU OR "PEASE L R"/AU OR ("PEASE
                 LARRY"/AU OR "PEASE LARRY R"/AU OR "PEASE LARRY READINGTON"/AU)
L3          4053 SEA ABB=ON  PLU=ON  RODRIGUEZ M?/AU
L4          7273 SEA ABB=ON  PLU=ON  MILLER D?/AU
L5           249 SEA ABB=ON  PLU=ON  PEASE L?/AU
L6             3 SEA ABB=ON  PLU=ON  L3 AND L4 AND L5
                 D STAT QUE
                 D IBIB ABS L6 1-3
L7             5 SEA ABB=ON  PLU=ON  SHIGM22 OR LIM (W)22 OR  SHIGM46 OR
                 EBVHIGM OR MSI19D10 OR  CB2BG8 OR AKJR4 OR CB2IE12 OR  CB2IE7
                 OR MSI(W) (19D10 OR 19(W)(D10 OR 'E5') OR 19E5) OR LYM46 OR
                 LYM(W)46 OR LIM22 OR MSI19E5
L8             3 SEA ABB=ON  PLU=ON  L7 NOT L6
                 D STAT QUE
                 D IBIB ABS L8 1-3

     FILE 'REGISTRY' ENTERED AT 14:30:33 ON 14 NOV 2005
L13            6 SEA ABB=ON  PLU=ON  SHIGM22
L14            2 SEA ABB=ON  PLU=ON  SHIGM46
L15            8 SEA ABB=ON  PLU=ON  EBVHIGM
L16            8 SEA ABB=ON  PLU=ON  MSI19D10
L17            4 SEA ABB=ON  PLU=ON  CB2BG8
L18            4 SEA ABB=ON  PLU=ON  AKJR4
L19            4 SEA ABB=ON  PLU=ON  CB2IE12
L20            4 SEA ABB=ON  PLU=ON  CB2IE7
L21            2 SEA ABB=ON  PLU=ON  MSI19E5

     FILE 'HCAPLUS' ENTERED AT 14:33:48 ON 14 NOV 2005

     FILE 'REGISTRY' ENTERED AT 14:33:48 ON 14 NOV 2005
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L22              SEL PLU=ON  L13 1- CHEM :      20 TERMS
                 SET SMARTSELECT OFF

     FILE 'HCAPLUS' ENTERED AT 14:33:49 ON 14 NOV 2005
L23            3 SEA ABB=ON  PLU=ON  L22

     FILE 'REGISTRY' ENTERED AT 14:34:50 ON 14 NOV 2005
                 SET SMARTSELECT ON
L24              SEL PLU=ON  L14 1- CHEM :       6 TERMS
                 SET SMARTSELECT OFF

     FILE 'HCAPLUS' ENTERED AT 14:34:50 ON 14 NOV 2005
L25            1 SEA ABB=ON  PLU=ON  L24

     FILE 'REGISTRY' ENTERED AT 14:34:57 ON 14 NOV 2005
                 SET SMARTSELECT ON
L26              SEL PLU=ON  L15 1- CHEM :      24 TERMS
                 SET SMARTSELECT OFF

     FILE 'HCAPLUS' ENTERED AT 14:34:58 ON 14 NOV 2005
L27            1 SEA ABB=ON  PLU=ON  L26

     FILE 'REGISTRY' ENTERED AT 14:36:07 ON 14 NOV 2005
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                SET SMARTSELECT ON
L28             SEL PLU=ON  L16 1- CHEM :      24 TERMS
                SET SMARTSELECT OFF

     FILE 'HCAPLUS' ENTERED AT 14:36:08 ON 14 NOV 2005
L29           2 SEA ABB=ON  PLU=ON  L28

     FILE 'REGISTRY' ENTERED AT 14:37:09 ON 14 NOV 2005
                SET SMARTSELECT ON
L30             SEL PLU=ON  L17 1- CHEM :      12 TERMS
                SET SMARTSELECT OFF

     FILE 'HCAPLUS' ENTERED AT 14:37:09 ON 14 NOV 2005
L31           1 SEA ABB=ON  PLU=ON  L30

     FILE 'REGISTRY' ENTERED AT 14:37:38 ON 14 NOV 2005
                SET SMARTSELECT ON
L32             SEL PLU=ON  L18 1- CHEM :      12 TERMS
                SET SMARTSELECT OFF

     FILE 'HCAPLUS' ENTERED AT 14:37:39 ON 14 NOV 2005
L33           1 SEA ABB=ON  PLU=ON  L32

     FILE 'REGISTRY' ENTERED AT 14:38:32 ON 14 NOV 2005
                SET SMARTSELECT ON
L34             SEL PLU=ON  L19 1- CHEM :      12 TERMS
                SET SMARTSELECT OFF

     FILE 'HCAPLUS' ENTERED AT 14:38:33 ON 14 NOV 2005
L35           1 SEA ABB=ON  PLU=ON  L34

     FILE 'REGISTRY' ENTERED AT 14:39:24 ON 14 NOV 2005
                SET SMARTSELECT ON
L36             SEL PLU=ON  L20 1- CHEM :      12 TERMS
                SET SMARTSELECT OFF

     FILE 'HCAPLUS' ENTERED AT 14:39:24 ON 14 NOV 2005
L37           1 SEA ABB=ON  PLU=ON  L36

     FILE 'REGISTRY' ENTERED AT 14:40:16 ON 14 NOV 2005
                SET SMARTSELECT ON
L38             SEL PLU=ON  L21 1- CHEM :       6 TERMS
                SET SMARTSELECT OFF

     FILE 'HCAPLUS' ENTERED AT 14:40:16 ON 14 NOV 2005
L39           1 SEA ABB=ON  PLU=ON  L38
L40           3 SEA ABB=ON  PLU=ON  L23 OR L25 OR L27 OR L29 OR L31 OR L33 OR
                L35 OR L37 OR L39
L41           1 SEA ABB=ON  PLU=ON  L40 NOT (L6 OR L8)
                D STAT QUE
                D IBIB ABS L41 1
L42        6099 SEA ABB=ON  PLU=ON  ?HIGM? OR MSI? OR CB2?
L43          11 SEA ABB=ON  PLU=ON  (L42 AND (L3 OR L4 OR L5)) NOT (L6 OR L8
                OR L41)
                D STAT QUE
                D IBIB ABS L43 1-11
L44           8 SEA ABB=ON  PLU=ON  ((L3 OR L4 OR L5) AND (RECOMB?(2A)(ANTIBOD?
                 OR AB OR ABS))) NOT (L6 OR L8 OR L41 OR L43)
                D STAT QUE
                D IBIB ABS L44 1-8
```

FILE HOME

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 13 NOV 2005 HIGHEST RN 867336-65-0
DICTIONARY FILE UPDATES: 13 NOV 2005 HIGHEST RN 867336-65-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

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**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from  *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
**********************************************************************
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Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE HCAPLUS

FILE COVERS 1907 - 14 Nov 2005 VOL 143 ISS 21
FILE LAST UPDATED: 13 Nov 2005 (20051113/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>

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=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 14:12:08 ON 14 NOV 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 14 Nov 2005  VOL 143 ISS 21
FILE LAST UPDATED: 13 Nov 2005  (20051113/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=>
=>

=> d stat que
L3          4053 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RODRIGUEZ M?/AU
L4          7273 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MILLER D?/AU
L5           249 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PEASE L?/AU
L6             3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 AND L4 AND L5


=>
=>

=> d ibib abs l6 1-3

L6   ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2003:777108  HCAPLUS
DOCUMENT NUMBER:          139:306535
TITLE:                    Human IgM antibodies for drug screening, diagnostic,
                          therapeutic uses against central nervous system
                          diseases
INVENTOR(S):              Rodriguez, Moses; Miller, David J.
                          ; Pease, Larry R.
PATENT ASSIGNEE(S):       Mayo Foundation, USA
SOURCE:                   U.S. Pat. Appl. Publ., 159 pp., Cont.-in-part of U.S.
                          Ser. No. 730,473.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   5
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     US 2003185827         A1    20031002    US 2001-10729           20011113
```

US 5591629	A	19970107	US 1994-236520	19940429
US 2002164325	A1	20021107	US 1997-779784	19970107
PRIORITY APPLN. INFO.:			US 1994-236520	A2 19940429
			US 1996-692084	A1 19960808
			US 1997-779784	A2 19970107
			US 1999-322862	B2 19990528
			US 2000-580787	B2 20000530
			US 2000-730473	A2 20001205
			US 1996-628380	A2 19960405

AB Antibodies, and particularly human antibodies, are disclosed that demonstrate activity in the treatment of demyelinating diseases as well as other diseases of the central nervous system that are of viral, bacterial or idiopathic origin, including neural dysfunction caused by spinal cord injury. Neuromodulatory agents are set forth that include and comprise a material selected from the group consisting of an antibody capable of binding structures or cells in the central nervous system, a peptide analog, a hapten, active fragments thereof, agonists thereof, mimics thereof, monomers thereof and combinations thereof. The neuromodulatory agent has one or more of the following characteristics: it is capable of inducing remyelination; binding to neural tissue; promoting Ca ++ signaling with oligodendrocytes; and promoting cellular proliferation of glial cells. Amino acid and DNA sequences of exemplary antibodies are disclosed. Methods are described for treating demyelinating diseases, and diseases of the central nervous system of humans and domestic animals, using polyclonal IgM antibodies and human monoclonal antibodies sHIgm22(LYM 22), sHIgm46(LYM46), ebvHIgM MSI19D10, CB2bG8, AKJR4, CB2iE12, CB2iE7, MSI19E5 and MSI10E10, active fragments thereof and the like. The invention also extends to the use of human antibodies, fragments, peptide derivs. and like materials, and their use in diagnostic and therapeutic applications, including screening assays for the discovery of addnl. antibodies that bind to cells of the nervous system, particularly oligodendrocytes.

L6 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2001:833383 HCAPLUS
DOCUMENT NUMBER:	135:370639
TITLE:	Human IgM antibodies with the capability of inducing remyelination, and diagnostic and therapeutic uses thereof particularly in the central nervous system
INVENTOR(S):	**Rodriguez, Moses; Miller, David J. ; Pease, Larry R.**
PATENT ASSIGNEE(S):	Mayo Foundation for Medical Education & research, USA
SOURCE:	PCT Int. Appl., 219 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085797	A1	20011115	WO 2000-US14902	20000530
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,				

CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2409515	AA	20011115	CA 2000-2409515	20000530
EP 1294770	A1	20030326	EP 2000-948498	20000530
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
BR 2000015875	A	20030624	BR 2000-15875	20000530
JP 2004516807	T2	20040610	JP 2001-582396	20000530
PRIORITY APPLN. INFO.:			US 2000-568351	A2 20000510
			WO 2000-US14902	W 20000530

AB Methods are described for treating demyelinating diseases in mammals, such as multiple sclerosis in humans, and viral diseases of the central nervous system of humans and domestic animals, such as post-infectious encephalomyelitis, or prophylactically inhibiting the initiation or progression of demyelination in these disease states, using human monoclonal autoantibodies characterized by their ability to bind structures and cells within the central nervous system. In particular, the methods utilize human monoclonal antibodies selected from the group of sHIgM22 (LIM 22), sHIgM46 ebvHIgM MSI19D10, CB2bG8, AKJR4, CB2iE12, CB2iE7 and MSI 19E5, monomers thereof, active fragments thereof and isolated or synthetic human or humanized autoantibodies having the characteristics of the foregoing. Nucleic acids and DNA mols. encoding the human monoclonal antibodies, or portions thereof, are provided. The invention also extends to the preparation and use of human polyclonal and monoclonal autoantibodies, monomers thereof, active fragments, peptide derivs. and fragments, and analogs, cognates, agonists and the like corresponding materials, and their use in diagnostic and therapeutic applications. For example, the autoantibodies, monomers, fragments, haptens, and peptide equivalent, are useful in the promotion of neural regeneration and neuroprotection, and therapeutic compns. and vaccines containing peptides or antibodies are included and presented.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1995:1003709 HCAPLUS
DOCUMENT NUMBER:	124:84348
TITLE:	Oligodendrocyte-reactive O1, O4, and HNK-1 monoclonal antibodies are encoded by germline immunoglobulin genes
AUTHOR(S):	Asakura, Kunihiko; **Miller, David J.**; Pogulis, Robert J.; **Pease, Larry R.**; **Rodriguez, Moses**
CORPORATE SOURCE:	Department of Neurology, Mayo Clinic and Foundation, 200 First St. SW, Rochester, MN, 55905, USA
SOURCE:	Molecular Brain Research (1995), 34(2), 283-93 CODEN: MBREE4; ISSN: 0169-328X
PUBLISHER:	Elsevier
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Natural or physiol. autoantibodies are present normally in serum, are polyreactive, are frequently of the IgM subtype, and are encoded by unmutated germline genes. The authors tested whether the oligodendrocyte-reactive O1, O4, A2B5, and HNK-1 IgMκ monoclonal antibodies are natural autoantibodies by sequencing Ig cDNAs and comparing these with published germline sequences. O1 VH was identical with unrearranged VH segment transcript A1 and A4. O4 VH had three and HNK-1 VH had six nucleotide differences from germline VH101 in the VH coding region. The D segment of O1 was derived from germline SP2 gene family. The D segments of O4 and HNK-1 were derived from DFL16 gene family. O4 JH and HNK-1 JH were encoded by unmutated germline JH4, whereas O1 JH was

encoded by germline JH1 with one silent nucleotide change. O1 and O4 light chains were identical with myeloma MOPC21 except for one silent nucleotide change. HNK-1 Vκ was identical with germline Vκ41 except for two silent nucleotide changes. O1 Jκ, O4 Jκ and HNK Jκ were encoded by unmutated germline Jκ2. In contrast, A2B5 VH showed seven nucleotide differences from germline V1, whereas no germline sequence encoding A2B5 Vκ was identified. O1 and O4, but not A2B5 were polyreactive against multiple antigens by direct ELISA. Therefore, O1, O4 and HNK-1 Igs are encoded by germline genes, and have the genotype and phenotype of natural autoantibodies.

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=> d stat que
L3          4053 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RODRIGUEZ M?/AU
L4          7273 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MILLER D?/AU
L5           249 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PEASE L?/AU
L6             3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 AND L4 AND L5
L7             5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SHIGM22 OR LIM (W)22 OR
                 SHIGM46 OR EBVHIGM OR MSI19D10 OR  CB2BG8 OR AKJR4 OR CB2IE12
                 OR  CB2IE7 OR MSI(W) (19D10 OR 19(W)(D10 OR 'E5') OR 19E5) OR
                 LYM46 OR LYM(W)46 OR LIM22 OR MSI19E5
L8             3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 NOT L6


=> d ibib abs l8 1-3

L8   ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:1124571  HCAPLUS
DOCUMENT NUMBER:          142:73412
TITLE:                    Recombinant human IgMs for promoting remyelination of
                          neurons and for diagnosing and treating demyelinating
                          diseases such as multiple sclerosis
INVENTOR(S):              Gruskin, Elliot A.; Chojnicki, Eric; Warrington,
                          Arthur E.; Bieber, Allan J.; Rodriguez, Moses
PATENT ASSIGNEE(S):       Mayo Foundation for Medical Education & Research, USA;
                          Acorda Therapeutics
SOURCE:                   PCT Int. Appl., 67 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND  DATE        APPLICATION NO.         DATE
     ---------------      ----  --------    --------------------    --------
     WO 2004110355         A2   20041223    WO 2004-US15436         20040517
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
PRIORITY APPLN. INFO.:                        US 2003-471235P     P  20030516
AB   Antibodies, and particularly human antibodies, are disclosed that
     demonstrate activity in the treatment of demyelinating diseases as well as
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other diseases of the central nervous system that are of viral, bacterial or idiopathic origin, including neural dysfunction caused by spinal cord injury. Neuromodulatory agents are set forth that include and comprise a material selected from the group consisting of an antibody capable of binding structures or cells in the central nervous system, a peptide analog, a hapten, active fragments thereof, agonists thereof, mimics thereof, monomers thereof and combinations thereof. Methods are described for treating demyelinating diseases, and diseases of the central nervous system of humans and domestic animals, using polyclonal IgM antibodies and human monoclonal antibodies **sHIgm22**(LYM 22), **sHIgm46**(**LYM46**) **ebvHIgM MSI19D10**, **CB2bG8**, **AKJR4**, **CB2iE12**, **CB2iE7**, **MSI19E5** and MSI10E10, active fragments thereof and the like. The invention also extends to the use of human antibodies, fragments, peptide derivs. and like materials, and their use in above referenced therapeutic applications, and to pharmaceutical compns. containing them, that may be administered in desirably low doses to treat conditions involving demyelination and to promote remyelination.

L8 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:60033 HCAPLUS
DOCUMENT NUMBER: 140:110128
TITLE: Dendritic cell function and immune response potentiation with a purified mol. that binds specifically to cell surface B7-DC polypeptides
INVENTOR(S): Pease, Larry R.; Rodriguez, Moses; Ure, Daren; Nguyen, Loc T.; Radhakrishnan, Suresh
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 26 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004014207	A1	20040122	US 2002-196601	20020716
WO 2004007679	A2	20040122	WO 2003-US21933	20030715
WO 2004007679	A3	20041014		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1543037	A2	20050622	EP 2003-764607	20030715
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005249737	A1	20051110	US 2005-178160	20050708
PRIORITY APPLN. INFO.:			US 2002-196601	A1 20020716
			WO 2003-US21933	W 20030715

AB A mol. capable of potentiating immune responses is described, as well as methods for using the mol. to enhance immune responses and enhance dendritic cell function. Preferably, the mol. is a human serum-derived antibody (sHIgM12). This antibody was shown to potentiate the

antigen-presenting function of dendritic cells. In a mouse model of B16 melanoma the sHIgM12 treatment was protective against lethal tumor challenge, it inhibited the tumor growth, and mice displayed persistent antitumor resistance. The inventors also produced a recombinant human IgM antibody (**sHIgM22**) and the same method was used to generate a recombinant supply of sHIgM12. Also described are compns. containing the mol. and methods for using the compns. to treat or immunize individuals.

L8 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:974396 HCAPLUS
DOCUMENT NUMBER: 140:109787
TITLE: Human monoclonal IgM antibody promotes CNS myelin repair independent of Fc function
AUTHOR(S): Ciric, Bogoljub; Howe, Charles L.; Soldan, Mateo Paz; Warrington, Arthur E.; Bieber, Allan J.; Van Keulen, Virginia; Rodriguez, Moses; Pease, Larry R.
CORPORATE SOURCE: Departments of Immunology, Mayo Clinic Rochester, MN, USA
SOURCE: Brain Pathology (2003), 13(4), 608-616
CODEN: BRPAE7; ISSN: 1015-6305
PUBLISHER: International Society of Neuropathology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The human monoclonal IgM antibody **sHIgM22** and mouse IgM monoclonal antibody 94.03 bind to oligodendrocytes, induce calcium signals in cultured glial cells, and promote remyelination in mouse models of multiple sclerosis. To address the mechanisms employed by these antibodies to promote CNS repair, bivalent monomers, F(ab')2 fragments, and monovalent forms of these antibodies were investigated to determine whether they exhibit the same remyelinating potential as the intact IgMs. The two antibodies displayed different structural requirements for retention of function. Antibody **sHIgM22** remained functional even when reduced to a bivalent F(ab')2 fragment, while disruption of the pentameric structure of antibody 94.03 destroyed its functional properties. Competition studies demonstrated that the two antibodies recognize different entities on the surface of glial cells. These results indicate that the constant region and pentameric structure of IgM is not always necessary for the stimulation of myelin repair, eliminating the requirement for IgM immune effector functions in this process. The ability of the antibodies to crosslink cell surface determinants on oligodendrocytes appears to be an essential aspect of the mechanism of cellular activation. The finding that two antibodies, which induce similar in vivo effects, bind to different structures, and have different crosslinking requirements suggests that activation of glial cells involves the rearrangement of a complex membrane compartment.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> => d stat que
L3 4053 SEA FILE=HCAPLUS ABB=ON PLU=ON RODRIGUEZ M?/AU
L4 7273 SEA FILE=HCAPLUS ABB=ON PLU=ON MILLER D?/AU
L5 249 SEA FILE=HCAPLUS ABB=ON PLU=ON PEASE L?/AU
L6 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L3 AND L4 AND L5
L7 5 SEA FILE=HCAPLUS ABB=ON PLU=ON SHIGM22 OR LIM (W)22 OR SHIGM46 OR EBVHIGM OR MSI19D10 OR CB2BG8 OR AKJR4 OR CB2IE12 OR CB2IE7 OR MSI(W) (19D10 OR 19(W)(D10 OR 'E5') OR 19E5) OR LYM46 OR LYM(W)46 OR LIM22 OR MSI19E5
L8 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L7 NOT L6
L13 6 SEA FILE=REGISTRY ABB=ON PLU=ON SHIGM22

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L14             2 SEA FILE=REGISTRY ABB=ON  PLU=ON  SHIGM46
L15             8 SEA FILE=REGISTRY ABB=ON  PLU=ON  EBVHIGM
L16             8 SEA FILE=REGISTRY ABB=ON  PLU=ON  MSI19D10
L17             4 SEA FILE=REGISTRY ABB=ON  PLU=ON  CB2BG8
L18             4 SEA FILE=REGISTRY ABB=ON  PLU=ON  AKJR4
L19             4 SEA FILE=REGISTRY ABB=ON  PLU=ON  CB2IE12
L20             4 SEA FILE=REGISTRY ABB=ON  PLU=ON  CB2IE7
L21             2 SEA FILE=REGISTRY ABB=ON  PLU=ON  MSI19E5
L22               SEL  PLU=ON  L13 1- CHEM :      20 TERMS
L23             3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L22
L24               SEL  PLU=ON  L14 1- CHEM :       6 TERMS
L25             1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L24
L26               SEL  PLU=ON  L15 1- CHEM :      24 TERMS
L27             1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L26
L28               SEL  PLU=ON  L16 1- CHEM :      24 TERMS
L29             2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L28
L30               SEL  PLU=ON  L17 1- CHEM :      12 TERMS
L31             1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L30
L32               SEL  PLU=ON  L18 1- CHEM :      12 TERMS
L33             1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L32
L34               SEL  PLU=ON  L19 1- CHEM :      12 TERMS
L35             1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L34
L36               SEL  PLU=ON  L20 1- CHEM :      12 TERMS
L37             1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36
L38               SEL  PLU=ON  L21 1- CHEM :       6 TERMS
L39             1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L38
L40             3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L23 OR L25 OR L27 OR L29 OR
                  L31 OR L33 OR L35 OR L37 OR L39
L41             1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L40 NOT (L6 OR L8)


=> d ibib abs l41 1

L41  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2000:412207  HCAPLUS
DOCUMENT NUMBER:          133:148908
TITLE:                    Human monoclonal antibodies reactive to
                          oligodendrocytes promote remyelination in a model of
                          multiple sclerosis
AUTHOR(S):                Warrington, Arthur E.; Asakura, Kunihiko; Bieber,
                          Allan J.; Ciric, Bogoljub; Van Keulen, Virginia;
                          Kaveri, Srini V.; Kyle, Robert A.; Pease, Larry R.;
                          Rodriguez, Moses
CORPORATE SOURCE:         Department of Neurology, Mayo Medical and Graduate
                          Schools, Rochester, MN, 55905, USA
SOURCE:                   Proceedings of the National Academy of Sciences of the
                          United States of America (2000), 97(12), 6820-6825
                          CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER:                National Academy of Sciences
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB    Promoting remyelination, a major goal of an effective treatment for
      demyelinating diseases, has the potential to protect vulnerable axons,
      increase conduction velocity, and improve neurol. deficits.  Strategies to
      promote remyelination have focused on transplanting oligodendrocytes (OLs)
      or recruiting endogenous myelinating cells with trophic factors.  Ig-based
      therapies, routinely used to treat a variety of neurol. and autoimmune
      diseases, underlie the authors' approach to enhance remyelination.  The
      authors isolated two human mAbs directed against OL surface antigens that
      promoted significant remyelination in a virus-mediated model of multiple
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sclerosis. Four addnl. OL-binding human mAbs did not promote remyelination. Both human mAbs were as effective as human i.v. Ig, a treatment shown to have efficacy in multiple sclerosis, and bound to the surface of human OLs suggesting a direct effect of the mAbs on the cells responsible for myelination. Alternatively, targeting human mAbs to areas of central nervous system (CNS) pathol. may facilitate the opsonization of myelin debris, allowing repair to proceed. Human mAbs were isolated from the sera of individuals with a form of monoclonal gammopathy. These individuals carry a high level of monoclonal protein in their blood without detriment, lending support to the belief that administration of these mAbs as a therapy would be safe. The authors' results are (i) consistent with the hypothesis that CNS-reactive mAbs, part of the normal Ig repertoire in humans, may help repair and protect the CNS from pathogenic immune injury, and (ii) further challenge the premise that Abs that bind OLs are necessarily pathogenic.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d hitstr

L41 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN
IT **287123-09-5**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(amino acid sequence; human monoclonal antibodies reactive to oligodendrocytes promote remyelination in model of multiple sclerosis)
RN 287123-09-5 HCAPLUS
CN Immunoglobulin M, anti-(human oligodendrocyte surface antigen) (human clone IgM22VH μ-chain V-D-J region) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> => d stat que

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L3          4053 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RODRIGUEZ M?/AU
L4          7273 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MILLER D?/AU
L5           249 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PEASE L?/AU
L6             3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 AND L4 AND L5
L7             5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SHIGM22 OR LIM (W)22 OR
                 SHIGM46 OR EBVHIGM OR MSI19D10 OR  CB2BG8 OR AKJR4 OR CB2IE12
                 OR  CB2IE7 OR MSI(W) (19D10 OR 19(W)(D10 OR 'E5') OR 19E5) OR
                 LYM46 OR LYM(W)46 OR LIM22 OR MSI19E5
L8             3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 NOT L6
L13            6 SEA FILE=REGISTRY ABB=ON  PLU=ON  SHIGM22
L14            2 SEA FILE=REGISTRY ABB=ON  PLU=ON  SHIGM46
L15            8 SEA FILE=REGISTRY ABB=ON  PLU=ON  EBVHIGM
L16            8 SEA FILE=REGISTRY ABB=ON  PLU=ON  MSI19D10
L17            4 SEA FILE=REGISTRY ABB=ON  PLU=ON  CB2BG8
L18            4 SEA FILE=REGISTRY ABB=ON  PLU=ON  AKJR4
L19            4 SEA FILE=REGISTRY ABB=ON  PLU=ON  CB2IE12
L20            4 SEA FILE=REGISTRY ABB=ON  PLU=ON  CB2IE7
L21            2 SEA FILE=REGISTRY ABB=ON  PLU=ON  MSI19E5
L22              SEL  PLU=ON  L13 1- CHEM :       20 TERMS
L23            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L22
L24              SEL  PLU=ON  L14 1- CHEM :        6 TERMS
L25            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L24
L26              SEL  PLU=ON  L15 1- CHEM :       24 TERMS
L27            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L26
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L28             SEL  PLU=ON  L16 1- CHEM :       24 TERMS
L29           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L28
L30             SEL  PLU=ON  L17 1- CHEM :       12 TERMS
L31           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L30
L32             SEL  PLU=ON  L18 1- CHEM :       12 TERMS
L33           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L32
L34             SEL  PLU=ON  L19 1- CHEM :       12 TERMS
L35           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L34
L36             SEL  PLU=ON  L20 1- CHEM :       12 TERMS
L37           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36
L38             SEL  PLU=ON  L21 1- CHEM :        6 TERMS
L39           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L38
L40           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L23 OR L25 OR L27 OR L29 OR
                L31 OR L33 OR L35 OR L37 OR L39
L41           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L40 NOT (L6 OR L8)
L42        6099 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ?HIGM? OR MSI? OR CB2?
L43          11 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L42 AND (L3 OR L4 OR L5))
                NOT (L6 OR L8 OR L41)


=> d ibib abs l43 1-11

L43  ANSWER 1 OF 11  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:1127898  HCAPLUS
DOCUMENT NUMBER:          142:273344
TITLE:                    Docking-based CoMFA and CoMSIA studies of
                          non-nucleoside reverse transcriptase inhibitors of the
                          pyridinone derivative type
AUTHOR(S):                Medina-Franco, J. L.; Rodriguez-Morales, S.;
                          Juarez-Gordiano, C.; Hernandez-Campos, A.; Castillo,
                          R.
CORPORATE SOURCE:         Departamento de Farmacia, Facultad de Quimica, UNAM,
                          CU, Mexico, DF 04510, Mex.
SOURCE:                   Journal of Computer-Aided Molecular Design (2004),
                          18(5), 345-360
                          CODEN: JCADEQ; ISSN: 0920-654X
PUBLISHER:                Kluwer Academic Publishers
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Comparative mol. field anal. (Co-MFA) and comparative mol. similarity
     indexes anal. (Co-MSIA) were performed on a set of pyridinone
     derivs.  A mol. alignment obtained by docking of compds. into the
     nonnucleoside reverse transcriptase inhibitor binding site of HIV-1 was
     used.  Good correlations between the calculated binding free energies and
     exptl. inhibitory activities suggest that the binding conformations of
     these inhibitors are reasonable.  Robust and predictive 3D-QSAR models
     were obtained with q2 values of 0.706 and 0.723 for Co-MFA and Co-
     MSIA, resp.  The models were validated by an external test set
     obtaining r2pred values of 0.720 and 0.750 for Co-MFA and Co-MSIA
     , resp.  The Co-MFA, Co-MSIA and docking results help to
     understand the type of interactions that occur between pyridinone derivs.
     with the nonnucleoside reverse transcriptase inhibitor binding pocket, and
     explain the viral resistance to pyridinone derivs. upon mutation of amino
     acids Tyr181 and Tyr188.  The results obtained provide information for a
     better understanding of the drug resistance mechanisms.  The 3D-QSAR
     models derived will be used to guide the design of pyridinone derivs.
     active against mutant strains of reverse transcriptase.
REFERENCE COUNT:          65    THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
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L43 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:815157 HCAPLUS
DOCUMENT NUMBER: 141:330606
TITLE: A human antibody that promotes remyelination enters the CNS and decreases lesion load as detected by T2-weighted spinal cord MRI in a virus-induced murine model of MS
AUTHOR(S): Pirko, Istvan; Ciric, Bogoljub; Gamez, Jeff; Bieber, Allan J.; Warrington, Arthur E.; Johnson, Aaron J.; Hanson, Dennis P.; **Pease, Larry R.**; Macura, Slobodan I.; **Rodriguez, Moses**
CORPORATE SOURCE: Dep. of Neurology, INMR Core Facility Mayo Clinic, Rochester, MN, 55905, USA
SOURCE: FASEB Journal (2004), 18(13), 1577-1579, 10.1096/fj.04-2026fje
CODEN: FAJOEC; ISSN: 0892-6638
PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The human monoclonal antibody **rHIgM22** enhances remyelination following spinal cord demyelination in a virus-induced murine model of multiple sclerosis. Using three-dimensional T2-weighted in vivo spinal cord magnetic resonance imaging (MRI), we have therefore assessed the extent of spinal cord demyelination, before and after 5 wk of treatment with **rHIgM22**, to determine whether antibody enhanced remyelination can be detected by MRI. A significant decrease was seen in T2 high signal lesion volume following antibody treatment. Histol. examination of the spinal cord tissue reveals that this decrease in lesion volume correlates with antibody promoted remyelination. To show that **rHIgM22** enters the spinal cord and colocalizes with demyelinating lesions, we used ultrasmall superparamagnetic iron oxide particle (USPIO)-labeled antibodies. This may be considered as addnl. evidence to the hypothesis that **rHIgM22** promotes remyelination by local effects in the lesions, likely by binding to CNS cells. The reduction in high signal T2-weighted lesion volume may be an important outcome measure in future clin. trials in humans.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:567553 HCAPLUS
DOCUMENT NUMBER: 141:172562
TITLE: Immunotherapeutic Potential of B7-DC (PD-L2) Cross-Linking Antibody In Conferring Antitumor Immunity
AUTHOR(S): Radhakrishnan, Suresh; Nguyen, Loc Tan; Ciric, Bogoljub; Flies, Dallas; Van Keulen, Virginia P.; Tamada, Koji; Chen, Lieping; **Rodriguez, Moses**; **Pease, Larry R.**
CORPORATE SOURCE: Departments of Immunology, Mayo Clinic College of Medicine, Mayo Clinic, Rochester, MN, USA
SOURCE: Cancer Research (2004), 64(14), 4965-4972
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A naturally occurring human antibody potentiates dendritic cell function on crosslinking B7-DC (PD-L2), supporting robust T-cell responses in vitro. Moreover, treatment of dendritic cells with B7-DC crosslinking

antibody resulted in secretion of interleukin-12, suggesting a TH1 polarization of this response. Here we show an in vivo immunotherapeutic effect of this B7-DC crosslinking antibody using a poorly immunogenic B16 melanoma tumor model. Treatment of mice systemically with antibody at the time of tumor cell engraftment prevented tumor growth in a CD4 and CD8 T-cell-dependent manner. The protective effect of B7-DC crosslinking antibody treatment was independent of endogenous antibody responses. Tumor-specific CTL precursors could be isolated from lymph nodes draining the tumor site in animals treated with B7-DC crosslinking antibody, but not from those treated with isotype control antibodies. The elicited antitumor responses in vivo were specific and long-lasting. More strikingly, treatment of mice with B7-DC crosslinking antibody after the tumors were established in the lungs resulted in protection in a CD8-, perforin-, and granzyme B-dependent fashion. Depletion of natural killer cells did not block the effects of treatment with B7-DC crosslinking antibody. Together, these findings demonstrate that crosslinking B7-DC with the human IgM antibody **sHIgM12** can induce a protective immune response against a weakly antigenic exptl. tumor and therefore has potential as a novel immunotherapeutic approach for treating cancer.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:545190 HCAPLUS

DOCUMENT NUMBER: 141:139029

TITLE: Blockade of Allergic Airway Inflammation Following Systemic Treatment with a B7-Dendritic Cell (PD-L2) Cross-Linking Human Antibody

AUTHOR(S): Radhakrishnan, Suresh; Iijima, Koji; Kobayashi, Takao; **Rodriguez, Moses**; Kita, Hirohito; **Pease, Larry R.**

CORPORATE SOURCE: Department of Immunology, Department of Internal Medicine, Mayo Clinic College of Medicine, Mayo Clinic, Rochester, MN, 55905, USA

SOURCE: Journal of Immunology (2004), 173(2), 1360-1365 CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors present a novel immunotherapeutic strategy using a human B7-DC crosslinking Ab that prevents lung inflammation, airway obstruction, and hyperreactivity to allergen in a mouse model of allergic inflammatory airway disease. Dendritic cells (DC) have the ability to skew the immune response toward a Th1 or Th2 polarity. The **sHIgM12** Ab functions in vitro by crosslinking the costimulatory family mol. B7-DC (PD-L2) on DC up-regulating IL-12 production, homing to lymph nodes, and T cell-activating potential of these APCs. Using chicken OVA as a model Ag, the administration of **sHIgM12** Ab to BALB/c mice blocked lung inflammation, airway pathol., and responsiveness to methacholine, even after animals were presensitized and a Th2-polarized immune response was established. This therapeutic strategy was ineffective in STAT4-deficient animals, indicating that IL-12 production is critical in this system. Moreover, the polarity of the immune response upon in vitro restimulation with Ag is changed in wild-type mice, with a resulting decrease in Th2 cytokines IL-4 and IL-5 and an increase in the immunoregulatory cytokine IL-10. These studies demonstrate that the immune response of hypersensitized responders can be modulated using B7-DC crosslinking Abs, preventing allergic airway disease upon re-exposure to allergen.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:523596 HCAPLUS
DOCUMENT NUMBER: 141:241733
TITLE: Neuron-binding human monoclonal antibodies support central nervous system neurite extension
AUTHOR(S): Warrington, Arthur E.; Bieber, Allan J.; van Keulen, Virginia; Ciric, Bogoljub; **Pease, Larry R.**; **Rodriguez, Moses**
CORPORATE SOURCE: Departments of Neurology, Mayo Clinic College of Medicine, Rochester, MN, USA
SOURCE: Journal of Neuropathology and Experimental Neurology (2004), 63(5), 461-473
CODEN: JNENAD; ISSN: 0022-3069
PUBLISHER: American Association of Neuropathologists, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two human IgMs (**sHIgM12** and **sHIgM42**) were identified that supported in vitro central nervous system (CNS) neurite extension equal to the potent neurite stimulatory mol. laminin. Both IgMs bound to multiple cell types in unfixed CNS tissue and to the surface of neurons in culture. Both monoclonal antibodies (mAbs) overrode the inhibitory effect of CNS mouse myelin on granule cell neurite extension. Neither mAb bound to the surface of mature oligodendrocytes or strictly colocalized with myelin proteins. Sialidase treatment eliminated the neuronal surface binding of both mAbs, whereas blocking sphingolipid synthesis with Fumonisin B1 or removing GPI-linked proteins with PIPLC did not. When used as substrates for mixed neuron/glia aggregates, **sHIgM12** and **sHIgM42** supported robust neurite extension while astrocytes remained in the aggregates. In contrast, laminin supported astrocyte migration and spreading. Human mAbs that support neurite extension are novel factors that may be of use in encouraging axon repair following injury while minimizing glial cell infiltration. Both human mAbs were isolated from individuals with monoclonal gammopathy. Each individual has carried high mAb titers in circulation for years without detriment. **SHIgM12** and **sHIgM42** are therefore unlikely to be systemically pathogenic.
REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:70726 HCAPLUS
DOCUMENT NUMBER: 140:355483
TITLE: Antiapoptotic signaling by a remyelination-promoting human antimyelin antibody
AUTHOR(S): Howe, Charles L.; Bieber, Allan J.; Warrington, Arthur E.; **Pease, Larry R.**; **Rodriguez, Moses**
CORPORATE SOURCE: Department of Neurology, Mayo Clinic and Foundation, Rochester, MN, 55905, USA
SOURCE: Neurobiology of Disease (2004), 15(1), 120-131
CODEN: NUDIEM; ISSN: 0969-9961
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Stabilizing the survival of oligodendrocytes and oligodendrocyte precursors within and near lesions in patients suffering from multiple sclerosis (MS) and other demyelinating diseases is an important therapeutic goal. Previous studies have identified a human-derived

monoclonal IgM antibody designated **rHIgM22** that induces remyelination in a mouse model of MS. The authors provide evidence that this antibody, directed against myelin, induces antiapoptotic signaling in premyelinating oligodendrocytes and reduces caspase-3 activation and caspase gene expression in mice undergoing antibody-induced remyelination. This effect was dependent on calcium entry via CNQX-sensitive channels and on lipid raft integrity, and was correlated with suppression of JNK signaling. Thus, **rHIgM22** may induce remyelination via rescue of oligodendrocytes, and such autoantibody-mediated signaling may have important therapeutic implications for a variety of neurol. diseases.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:1011006 HCAPLUS
DOCUMENT NUMBER: 140:215843
TITLE: Antibody-mediated remyelination operates through mechanism independent of immunomodulation
AUTHOR(S): Ciric, Bogoljub; Van Keulen, Virginia; Paz Soldan, Mateo; **Rodriguez, Moses; Pease, Larry R.**
CORPORATE SOURCE: Department of Immunology, Mayo Clinic College of Medicine, Rochester, MN, 55905, USA
SOURCE: Journal of Neuroimmunology (2004), 146(1-2), 153-161
CODEN: JNRIDW; ISSN: 0165-5728
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A set of antibodies capable of binding glial cells promotes remyelination in models of multiple sclerosis (MS). Within this set, the mouse antibody, SCH94.03, was immunomodulatory implying that immune system mobilization might be integral to remyelination. The authors evaluated whether the human remyelination-promoting antibody **rHIgM22** influences acquired immunity. The antibody did not bind to immune cells, or influence humoral immune responses, antigen presentation, T cell proliferation or cytokine production Treatment with **rHIgM22** had no effect on demyelination or virus infection in two disease models. These results demonstrate that the remyelination-promoting activity of antibody **rHIgM22** is not dependent on immunomodulation.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:129168 HCAPLUS
DOCUMENT NUMBER: 138:168453
TITLE: Naturally Occurring Human IgM Antibody That Binds B7-DC and Potentiates T Cell Stimulation by Dendritic Cells
AUTHOR(S): Radhakrishnan, Suresh; Nguyen, Loc T.; Ciric, Bogoljub; Ure, Daren R.; Zhou, Bin; Tamada, Koji; Dong, Haidong; Tseng, Su-Yi; Shin, Tahiro; Pardoll, Drew M.; Chen, Lieping; Kyle, Robert A.; **Rodriguez, Moses; Pease, Larry R.**
CORPORATE SOURCE: Mayo Medical and Graduate Schools, Department of Immunology, Mayo Clinic, Rochester, MN, 55905, USA
SOURCE: Journal of Immunology (2003), 170(4), 1830-1838
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A human IgM Ab, serum-derived human IgM 12 (**sHIgM12**), is identified that binds mouse and human dendritic cells (DC), inducing dramatic immunopotentiation following treatment of the mouse DC in vitro. Competition, transfection, and knockout studies identified the ligand on mouse DC as the costimulatory mol. family member B7-DC. Potent T cell responses are stimulated by Ag-pulsed DC treated with the **sHIgM12** Ab in vitro and upon adoptive transfer of Ab-treated Ag-pulsed DC into animals. The multivalent structure of pentameric IgM provides the potential for crosslinking cell surface targets, endowing the soluble Abs with biol. potential not normally associated with immune function. The ability of the **sHIgM12** Ab to potentiate the immune response is dependent on the multimeric structure of IgM, as bivalent monomers do not retain this property. Furthermore, pretreatment of DC with IgM monomers blocks subsequent potentiation by intact IgM pentamers, an indication that crosslinking of B7-DC on the cell surface is critical for potentiation of Ag presentation. These findings imply that, in addition to known costimulatory roles, B7-DC can function as a receptor for signals delivered by cells expressing B7-DC ligands.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:897174 HCAPLUS

DOCUMENT NUMBER: 138:3641

TITLE: Cross-linking the B7 family molecule B7-DC directly activates immune functions of dendritic cells

AUTHOR(S): Nguyen, Loc T.; Radhakrishnan, Suresh; Ciric, Bogoljub; Tamada, Koji; Shin, Tahiro; Pardoll, Drew M.; Chen, Lieping; **Rodriguez, Moses**; **Pease, Larry R.**

CORPORATE SOURCE: Department of Immunology, Mayo Medical and Graduate Schools, Mayo Clinic, Rochester, MN, 55905, USA

SOURCE: Journal of Experimental Medicine (2002), 196(10), 1393-1398
CODEN: JEMEAV; ISSN: 0022-1007

PUBLISHER: Rockefeller University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB B7-DC mols. are known to function as ligands on antigen-presenting cells (APCs), enhancing T cell activation. In this study, crosslinking B7-DC with the monoclonal antibody **sHIgM12** directly potentiates dendritic cell (DC) function by enhancing DC presentation of major histocompatibility complex-peptide complexes, promoting DC survival; and increasing secretion of interleukin (IL)-12p70, a key T helper cell type 1 promoting cytokine. Furthermore, ex vivo treatment of DCs or systemic treatment of mice with **sHIgM12** increases the number of transplanted DCs that reach draining lymph nodes and increases the ability of lymph node APCs to activate naive T cells. Systemic administration of the antibody has an equivalent effect on DCs transferred at a distant site. These findings implicate B7-DC expressed on DCs in bidirectional communication. In addition to the established costimulatory and inhibitory functions associated with B7-DC, this mol. can also function as a conduit for extracellular signals to DCs modifying Dc functions.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:571782 HCAPLUS

DOCUMENT NUMBER: 137:153595

TITLE: Direct evidence that a human antibody derived from patient serum can promote myelin repair in a mouse model of chronic-progressive demyelinating disease
AUTHOR(S): Mitsunaga, Yoshihiro; Ciric, Bogoljub; Van Keulen, Virginia; Warrington, Arthur E.; Paz Soldan, M. Mateo; Bieber, Allan J.; **Rodriguez, Moses**; **Pease, Larry R.**
CORPORATE SOURCE: Department of Neurology, Mayo Medical and Graduate Schools, Mayo Clinic, Rochester, MN, USA
SOURCE: FASEB Journal (2002), 16(10), 1325-1327, 10.1096/fj.01-0994fje
CODEN: FAJOEC; ISSN: 0892-6638
PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Certain human sera from patients with monoclonal gammopathies contain factors that induce myelin repair in animals with demyelinating disease. The authors hypothesize that antibodies functionally distinguish the serum of one patient from another. However, pooled normal polyclonal human IgM antibodies also induce remyelination. Definitive proof that specific antibodies are the biol. active components of serum is missing because unquestionably pure prepns. of antibody mols. cannot be generated by fractionation. To demonstrate definitively that antibody is the biol. active component of patient serum, recombinant antibody was generated for evaluation in bioassays. The induction of remyelination in vivo requires milligram quantities of antibody. Consequently, an expression system was engineered to express high-titer, recombinant human IgM antibodies in vitro. A resulting recombinant antibody (**rHIgM22**) was evaluated for its ability to induce remyelination in the Theiler's virus mouse model of chronic-progressive demyelinating disease. The authors demonstrate that a single recombinant monoclonal antibody recapitulates the key characteristics of patient serum, including binding specificity, the induction of calcium signals in oligodendrocytes in vitro, and the induction of myelin repair within demyelinated plaques in vivo. The **rHIgM22** antibody provides a new venue for the anal. of mechanisms governing remyelination and may prove useful in the treatment of demyelinating diseases.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:227331 HCAPLUS
DOCUMENT NUMBER: 135:3795
TITLE: Microsatellite instability occurs in distinct subtypes of pediatric but not adult central nervous system tumors
AUTHOR(S): Alonso, Michelle; Hamelin, Richard; Kim, Mimi; Porwancher, Kara; Sung, Tammy; Parhar, Preeti; **Miller, Douglas C.**; Newcomb, Elizabeth W.
CORPORATE SOURCE: Department of Pathology, New York University School of Medicine, New York, NY, 10016, USA
SOURCE: Cancer Research (2001), 61(5), 2124-2128
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Length alterations in microsatellite repeats, termed microsatellite instability (**MSI**), are found in 10-15% of sporadic colon, endometrial, and gastric cancers harboring defects in DNA mismatch repair

(MMR) genes. We used the microsatellite markers Big Adenine Tract (BAT) 26 and BAT-25 from the reference panel of five markers recommended by the National Cancer Institute to evaluate the incidence of **MSI** in 206 central nervous system tumors. We screened 102 pediatric and 104 adult cases representing 165 astrocytic and 41 nonastrocytic tumors. The overall incidence of **MSI** was 8% (16 of 206). All 16 tumors with **MSI** were found in pediatric rather than adult patients. **MSI** was associated with two distinct subtypes of pediatric tumors occurring in 27% (12 of 45) of WHO grade III and grade IV astrocytomas and 24% (4 of 17) of gangliogliomas. We evaluated the difference in clinicopathol. and genetic features among 45 high-grade pediatric astrocytomas by **MSI** status. The median survival for pediatric patients with **MSI** (n = 12) was 8 mo compared with 15 mo for those patients without **MSI** (n = 33; P = 0.18). The frequency of p53 gene mutations was 13% for pediatric patients with **MSI** (n = 8) compared with 47% for those patients without **MSI** (n = 19; P = 0.19). These results revealed a trend between **MSI** status and prognosis and **MSI** status and frequency of p53 gene mutations. Our data suggest that pediatric high-grade astrocytomas can be attributed to two different genetic pathways: a MMR-deficient pathway and a MMR-proficient pathway.

REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> => d stat que
L3          4053 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RODRIGUEZ M?/AU
L4          7273 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MILLER D?/AU
L5           249 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PEASE L?/AU
L6             3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 AND L4 AND L5
L7             5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SHIGM22 OR LIM (W)22 OR
                 SHIGM46 OR EBVHIGM OR MSI19D10 OR  CB2BG8 OR AKJR4 OR CB2IE12
                 OR  CB2IE7 OR MSI(W) (19D10 OR 19(W)(D10 OR 'E5') OR 19E5) OR
                 LYM46 OR LYM(W)46 OR LIM22 OR MSI19E5
L8             3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 NOT L6
L13            6 SEA FILE=REGISTRY ABB=ON  PLU=ON  SHIGM22
L14            2 SEA FILE=REGISTRY ABB=ON  PLU=ON  SHIGM46
L15            8 SEA FILE=REGISTRY ABB=ON  PLU=ON  EBVHIGM
L16            8 SEA FILE=REGISTRY ABB=ON  PLU=ON  MSI19D10
L17            4 SEA FILE=REGISTRY ABB=ON  PLU=ON  CB2BG8
L18            4 SEA FILE=REGISTRY ABB=ON  PLU=ON  AKJR4
L19            4 SEA FILE=REGISTRY ABB=ON  PLU=ON  CB2IE12
L20            4 SEA FILE=REGISTRY ABB=ON  PLU=ON  CB2IE7
L21            2 SEA FILE=REGISTRY ABB=ON  PLU=ON  MSI19E5
L22              SEL  PLU=ON  L13 1- CHEM :      20 TERMS
L23            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L22
L24              SEL  PLU=ON  L14 1- CHEM :       6 TERMS
L25            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L24
L26              SEL  PLU=ON  L15 1- CHEM :      24 TERMS
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L28              SEL  PLU=ON  L16 1- CHEM :      24 TERMS
L29            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L28
L30              SEL  PLU=ON  L17 1- CHEM :      12 TERMS
L31            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L30
L32              SEL  PLU=ON  L18 1- CHEM :      12 TERMS
L33            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L32
L34              SEL  PLU=ON  L19 1- CHEM :      12 TERMS
L35            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L34
L36              SEL  PLU=ON  L20 1- CHEM :      12 TERMS
L37            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36
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L38             SEL  PLU=ON  L21 1- CHEM :        6 TERMS
L39           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L38
L40           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L23 OR L25 OR L27 OR L29 OR
                L31 OR L33 OR L35 OR L37 OR L39
L41           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L40 NOT (L6 OR L8)
L42        6099 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ?HIGM? OR MSI? OR CB2?
L43          11 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L42 AND (L3 OR L4 OR L5))
                NOT (L6 OR L8 OR L41)
L44           8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ((L3 OR L4 OR L5) AND
                (RECOMB?(2A)(ANTIBOD? OR AB OR ABS))) NOT (L6 OR L8 OR L41 OR
                L43)


=> d ibib abs l44 1-8

L44  ANSWER 1 OF 8  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:39567  HCAPLUS
DOCUMENT NUMBER:          142:353929
TITLE:                    Transient expression in tobacco leaves of an
                          aglycosylated recombinant antibody
                          against the epidermal growth factor receptor
AUTHOR(S):                Rodriguez, Meilyn; Ramirez, Nadia I.; Ayala,
                          Marta; Freyre, Freya; Perez, Lincidio; Triguero, Ada;
                          Mateo, Cristina; Selman-Housein, Guillermo; Gavilondo,
                          Jorge V.; Pujol, Merardo
CORPORATE SOURCE:         Center for Genetic Engineering and Biotechnology
                          (CIGB), Havana, 10600, Cuba
SOURCE:                   Biotechnology and Bioengineering (2004), Volume Date
                          2005, 89(2), 188-194
                          CODEN: BIBIAU; ISSN: 0006-3592
PUBLISHER:                John Wiley & Sons, Inc.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   When generating stably transformed transgenic plants, transient gene
     expression expts. are especially useful to rapidly confirm that the foreign
mol.
     of interest is correctly assembled and retains its biol. activity.
     TheraCIM (CIMAB S.A., Havana) is a recombinant humanized
     antibody against the Epidermal Growth Factor receptor (EGF-R), now
     in clin. trials for cancer therapy in Cuba and other countries.  An
     aglycosylated version (Asn 297 was mutated for Gln 297) of this antibody
     was transiently expressed in tobacco leaves after vacuum-mediated
     infiltration of recombinant Agrobacterium tumefaciens that carried a
     binary plasmid bearing the antibody heavy and light chain genes and plant
     regulation signals.  Protein exts. from "agroinfiltrated" leaves were
     tested by ELISA and Western blot, showing that the fully assembled
     antibody was accumulated in plant tissues.  The absence of plant specific
     glycans did not interfere in the assembling or in the activity of the
     plantibody, as demonstrated in this work.  Indirect immunofluorescence
     demonstrated that the aglycosylated antibody expressed in plants
     recognizes the EGF-R expressed on the surface of A431 human tumor culture
     cells.
REFERENCE COUNT:          36    THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44  ANSWER 2 OF 8  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:749021  HCAPLUS
DOCUMENT NUMBER:          142:52440
TITLE:                    Onchocerca volvulus: expression and immunolocalization
                          of a nematode cathepsin D-like lysosomal aspartic
```

protease
AUTHOR(S): Jolodar, Abbas; Fischer, Peter; Buettner, Dietrich W.; **Miller, David J.**; Schmetz, Christel; Brattig, Norbert W.
CORPORATE SOURCE: Tropical Medicine Section, Bernhard Nocht Institute for Tropical Medicine, Hamburg, 20359, Germany
SOURCE: Experimental Parasitology (2004), 107(3/4), 145-156
CODEN: EXPAAA; ISSN: 0014-4894
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The N-terminal region of the cathepsin D-like aspartic protease from the human filarial parasite Onchocerca volvulus was expressed as His-tag fusion protein. Light and electron microscopic immunohistol. using **antibodies** against the **recombinant** protein showed labeling of lysosomes in the hypodermis and epithelia of the intestine and the reproductive organs of Onchocerca. While developing oocytes were neg., mature oocytes and early morulae showed strong labeling. In older embryos and mature microfilariae, stained lysosomes were only found in a few cells. Cell death in degenerating microfilariae of patients untreated and treated with microfilaricidal drugs was associated with strong expression of aspartic protease. IgG1, IgG4, and IgE antibodies reactive with the recombinant protein were demonstrated in sera from onchocerciasis patients indicating exposure and recognition of the enzyme by the host's defense system. The aspartic protease of O. volvulus appears to function in intestinal digestion and tissue degradation of the filaria.
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:384647 HCAPLUS
DOCUMENT NUMBER: 140:373347
TITLE: Targeting kallikrein 6 proteolysis attenuates CNS inflammatory disease
AUTHOR(S): Blaber, Sachiko I.; Ciric, Bogoljub; Christophi, Geroge P.; Bernett, Matthew J.; Blaber, Michael; **Rodriguez, Moses**; Scarisbrick, Isobel A.
CORPORATE SOURCE: Institute of Molecular Biophysics, Department of Chemistry and Biochemistry, Florida State University, Tallahassee, FL, 32306-4380, USA
SOURCE: FASEB Journal (2004), 18(7), 920-922, 10.1096/fj.03-1212fje
CODEN: FAJOEC; ISSN: 0892-6638
PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Kallikrein 6 (K6, MSP) is a newly identified member of the Kallikrein family of serine proteases that is preferentially expressed in the adult central nervous system (CNS). We have previously demonstrated that K6 is abundantly expressed by inflammatory cells at sites of CNS inflammation and demyelination in animal models of multiple sclerosis (MS), and in human MS lesions. To test the hypothesis that this novel enzyme is a mediator of pathogenesis in CNS inflammatory disease, we have evaluated whether autonomously generated K6 antibodies alter the clinicopathol. course of disease in murine proteolipid protein139-151-induced exptl. autoimmune encephalomyelitis (PLP139-151 EAE). We demonstrate that immunization of mice with **recombinant** K6 generates **antibodies** that block K6 enzymic activity in vitro, including the breakdown of myelin basic protein (MBP), and that K6-immunized mice

exhibit significantly delayed onset and severity of clin. deficits. Reduced clin. deficits were reflected in significantly less spinal cord pathol. and meningeal inflammation and in reduced Th1 cellular responses in vivo and in vitro. These data demonstrate for the first time that K6 participates in enzymic cascades mediating CNS inflammatory disease and that this unique enzyme may represent a novel therapeutic target for the treatment of progressive inflammatory disorders, including MS.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:145863 HCAPLUS
DOCUMENT NUMBER: 140:422233
TITLE: Transient expression of a full-size antibody against hepatitis B surface antigen in plant cell suspension cultures
AUTHOR(S): **Rodriguez, Meilyn**; Ramirez, Nadia I.; Gongora, Walter; Fuentes, Alejandro; Perez, Marlene; Ayala, Marta; Gavilondo, Jorge V.; Selman-Housein, Guillermo
CORPORATE SOURCE: Plant Division, Centre for Genetic Engineering and Biotechnology, Havana, 10600, Cuba
SOURCE: Biotecnologia Aplicada (2003), 20(3), 152-154
CODEN: BTAPEP; ISSN: 0864-4551
PUBLISHER: Elfos Scientiae
DOCUMENT TYPE: Journal; (computer optical disk)
LANGUAGE: English

AB When generating stably transformed transgenic plants, transient gene expression expts. are especially useful to confirm that the foreign mol. of interest is expressed with an adequate biol. activity. In this paper the authors report the transient expression of a full-size mouse monoclonal antibody against Hepatitis B surface antigen in tobacco cell suspension cultures. Transient expression in tobacco cell cultures was fast, and protein expression could be detected in just a few days. The authors were able to verify that the gene construction was functional, and that 0.3-0.5 μg of a biol. active antibody was easily purified from 1 mL of cell culture by Protein A chromatog. Recovered **recombinant antibodies** were sufficient for a detailed characterization by SDS-PAGE, Western-blot, and ELISA. These results allowed the authors to move on to the large-scale production of the plantibody in stably transformed transgenic plants.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:986708 HCAPLUS
DOCUMENT NUMBER: 140:252032
TITLE: Monoclonal **Antibodies** to the **Recombinant** Protein TmpA of the Treponema pallidum
AUTHOR(S): Brito Moreno, Adys I.; Acosta Bas, Carmen; **Rodriguez, Maya**; Baluja Conde, Ileana B.; Feal Carballo, Sadys; Martinez, Luisa
CORPORATE SOURCE: Centro de Inmunoensayo, Laboratorio de Anticuerpos Monoclonales, Ciudad Habana, Cuba
SOURCE: Hybridoma and Hybridomics (2003), 22(6), 393-396
CODEN: HHYYBF; ISSN: 1536-8599
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Spleen cells from BALB/c mice immunized with recombinant TmpA were fused with mouse myeloma cells (P3/X63-Ag8), and five hybridomas secreting monoclonal antibodies were obtained. These hybridomas specifically recognize TmpA and do not cross-react with other mols. such as recombinant HBsAg of HBV and synthetic HCV core peptides. The monoclonal antibodies were IgG1 subclass and ascitic fluid from these hybridomas was purified by affinity chromatog. on Protein A-Sepharose CL-4B column to isolate the IgG1 active fraction. The affinity constant of these monoclonal antibodies ranged from 6.4 + 108 and 1.73 + 1010 M-1.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:196153 HCAPLUS

DOCUMENT NUMBER: 137:246269

TITLE: Targeting of adenovirus to endothelial cells by a bispecific single-chain diabody directed against the adenovirus fiber knob domain and human endoglin (CD105)

AUTHOR(S): Nettelbeck, Dirk M.; **Miller, Daniel W.**; Jerome, Valerie; Zuzarte, Marylou; Watkins, Sarah J.; Hawkins, Robert E.; Muller, Rolf; Kontermann, Roland E.

CORPORATE SOURCE: Institut fur Molekularbiologie und Tumorforschung, Philipps-Universitat Marburg, Marburg, D-35033, Germany

SOURCE: Molecular Therapy (2001), 3(6), 882-891
CODEN: MTOHCK; ISSN: 1525-0016

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The use of adenoviruses for antivascular cancer gene therapy is limited by their low transduction efficiency for endothelial cells. The authors have developed a **recombinant** bispecific **antibody** as a mol. bridge, linking the adenovirus capsid to the endothelial cell surface protein endoglin, for vascular targeting of adenoviruses. Endoglin (CD105), a component of the transforming growth factor β receptor complex, represents a promising target for antivascular cancer therapy. Endoglin is expressed predominantly on endothelial cells and is upregulated in angiogenic areas of tumors. The authors isolated single-chain Fv fragments directed against human endoglin from a human semisynthetic antibody library. One of the isolated scFv fragments (scFv C4) bound specifically to various proliferating primary endothelial cells or cell lines including HUVEC, HDMEC, HMVEC, and HMEC. ScFv C4 was therefore used to construct a bispecific single-chain diabody directed against endoglin and the adenovirus fiber knob domain (scDb EDG-Ad). This bispecific mol. mediated enhanced and selective adenovirus transduction of HUVECs, which was independent from binding to the coxsackievirus and adenovirus receptor (CAR) and αv-integrins. Thus, adenovirus infection was redirected to a new cellular receptor (CD105) and cell entry pathway. These results demonstrate the utility of bispecific single-chain diabodies, which can be produced in large quantities in bacteria, for the retargeting of adenoviruses in cancer gene therapy. (c) 2001 Academic Press.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:74747 HCAPLUS

DOCUMENT NUMBER: 134:279239

TITLE: Antigens to viral capsid and non-capsid proteins are present in brain tissues and antibodies in sera of Theiler's virus-infected mice
AUTHOR(S): Cameron, K.; Zhang, X.; Seal, B.; **Rodriguez, M.**; Njenga, M. K.
CORPORATE SOURCE: Department of Veterinary Pathobiology, University of Minnesota, St. Paul, MN, 55108, USA
SOURCE: Journal of Virological Methods (2001), 91(1), 11-19
CODEN: JVMEDH; ISSN: 0166-0934
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Recombinant proteins to the LP, VP1, VP2, VP3, VP4, 2A, 2B, 2C, 3A, and 3D genes of Theiler's murine encephalomyelitis virus (TMEV) were generated and antibodies were produced against them for use in anal. of the TMEV epitopes responsible for eliciting the antibody responses observed during acute and chronic disease. **Antibodies** against **recombinant** VP1, VP2, and VP3 recognized the corresponding proteins from purified TMEV particles. In immunohistochem. anal., **antibodies** against **recombinant** capsid (VP1, VP2, and VP3), and non-capsid (2A, 2C, 3A) proteins were reactive with PO-2D cells (astrocytes) infected with TMEV in vitro and with brain tissues of acutely infected mice. Antibodies against VP4, 2B, and 3D antigens were not reactive with corresponding viral proteins in infected astrocytes cells or brain tissues, but they reacted with TMEV precursor proteins produced during the early viral replication phase. Sera from SJL/J mice infected with TMEV acutely (14 days) and chronically (45 days) reacted with VP1, VP2, VP4, 2A, and 2C proteins. In an in vitro assay for neutralization, only anti-VP1 antibodies neutralized TMEV infection. These findings suggest that both capsid and non-capsid proteins of TMEV play a role in the immunopathol. of the TMEV disease in the central nervous system.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:214725 HCAPLUS
DOCUMENT NUMBER: 120:214725
TITLE: Identification and characterization of a novel repetitive antigen from Onchocerca spp.
AUTHOR(S): Catmull, Julian; Zhang, Dan; Ruggiero, Florence; Copeman, David B.; **Miller, David J.**
CORPORATE SOURCE: Dep. Chem. Biochem., James Cook Univ. North Queensland, Townsville, 4811, Australia
SOURCE: Molecular and Biochemical Parasitology (1994), 63(1), 49-57
CODEN: MBIPDP; ISSN: 0166-6851
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A novel repetitive antigen from the cattle parasite Onchocerca gibsoni was shown to be recognized by sera from humans infected with Oncocerca volvulus, Wuchereria bancroftii or Brugia malayi. The O. gibsoni protein was produced in a **recombinant** form, and **antibodies** raised to this protein used to screen cDNA libraries for O. volvulus. A series of clones were isolated which encoded repetitive regions very similar to those in O. gibsoni, but interspersed between these were longer repeating units which the authors have not so far found in O. gibsoni. The repetitive antigen was shown to be of high mol. weight and present only in the insol. (membrane) fraction of O. gibsoni microfilaria. Immunofluorescence techniques demonstrated that the antigen was associated both with muscle and with specific membrane layers, including a peripheral

layer which corresponds to either the outer hypodermis or an inner region of the cuticle in adult female O. gibsoni. In many respects, the proteins encoded by the O. gibsoni and O. volvulus cDNA clones resembled repetitive antigens from several distantly related eukaryotic parasites, and a possible common role in immune evasion is discussed.

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? SHOW FILES
File 155:MEDLINE(R) 1951-2005/Nov 11
         (c) format only 2005 Dialog
File   5:Biosis Previews(R) 1969-2005/Nov W1
         (c) 2005 BIOSIS
File  34:SciSearch(R) Cited Ref Sci 1990-2005/Nov W1
         (c) 2005 Inst for Sci Info
File  71:ELSEVIER BIOBASE 1994-2005/Nov W2
         (c) 2005  Elsevier Science B.V.
File  73:EMBASE 1974-2005/Nov 14
         (c) 2005 Elsevier Science B.V.
File 351:Derwent WPI 1963-2005/UD,UM &UP=200572
         (c) 2005  Thomson Derwent
File 357:Derwent Biotech Res. _1982-2005/Nov W2
         (c) 2005 Thomson Derwent & ISI
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? DS

Set     Items   Description
S1         15   SHIGM22 OR LYM22 OR LIM22 OR (LIM OR LYM OR SHIGM OR HIGM)-
              (W)22
S2          9   RD (unique items)
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?
? T S2/3 AB/1-9

 2/AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2005 Dialog. All rts. reserv.

15095201   PMID: 14655764
  Human  monoclonal  IgM antibody promotes CNS myelin repair independent of
Fc function.
  Ciric  Bogoljub;  Howe  Charles L; Paz Soldan Mateo; Warrington Arthur E;
Bieber Allan J; Van Keulen Virginia; Rodriguez Moses; Pease Larry R
  Department  of Immunology, Mayo Medical and Graduate Schools, Mayo Clinic
Rochester, Minn 55905, USA.
  Brain  pathology (Zurich, Switzerland) (Switzerland)   Oct 2003,  13  (4)
 p608-16,  ISSN 1015-6305   Journal Code: 9216781
  Contract/Grant No.: R01 NS24180; NS; NINDS
  Publishing Model Print
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: MEDLINE; Completed
  The  human monoclonal IgM antibody sHIgM22 and mouse IgM monoclonal
antibody 94.03 bind to oligodendrocytes, induce calcium signals in cultured
glial cells,  and promote remyelination in mouse models of multiple
sclerosis.  In order to address the mechanisms employed by these antibodies
to promote CNS repair, bivalent monomers, F(ab')2 fragments, and monovalent
forms  of  these  antibodies  were  investigated  to determine whether they
exhibit  the  same  remyelinating  potential  as  the  intact IgMs. The two
antibodies  displayed  different  structural  requirements for retention of
function. Antibody sHIgM22 remained functional even when reduced to a
bivalent  F(ab')2 fragment, while disruption of the pentameric structure of
antibody  94.03  destroyed  its  functional properties. Competition studies
demonstrated  that  the  two antibodies recognize different entities on the
surface of glial cells. These results indicate that the constant region and
pentameric  structure of IgM is not always necessary for the stimulation of
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myelin repair, eliminating the requirement for IgM immune effector functions in this process. The ability of the antibodies to cross-link cell surface determinants on oligodendrocytes appears to be an essential aspect of the mechanism of cellular activation. The finding that two antibodies, which induce similar in vivo effects, bind to different structures, and have different cross-linking requirements suggests that activation of glial cells involves the rearrangement of a complex membrane compartment.

2/AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14083557 PMID: 11857682
Human antibodies accelerate the rate of remyelination following lysolecithin-induced demyelination in mice.
Bieber Allan J; Warrington Arthur; Asakura Kuni; Ciric Bogoljub; Kaveri Srini V; Pease Larry R; Rodriguez Moses
Department of Neurology, Mayo Medical and Graduate Schools, Rochester, Minnesota 55905, USA. bieber.allan@mayo.edu
Glia (United States) Mar 1 2002, 37 (3) p241-9, ISSN 0894-1491
Journal Code: 8806785
Contract/Grant No.: NS24180; NS; NINDS
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Immunoglobulin-based therapies are becoming increasingly common for the treatment of neurologic and autoimmune diseases in humans. In this study, we demonstrate that systemic administration of either polyclonal human immunoglobulins or specific human monoclonal antibodies can accelerate the rate of CNS remyelination following toxin-induced demyelination. Injection of lysolecithin directly into the spinal cord results in focal demyelinated lesions. In contrast to other murine models of demyelinating disease, the mechanism of demyelination following lysolecithin injection is independent of immune system activation, and chronic inflammation at the site of the lesion is minimal. Administration of polyclonal human IgM (pHIgM) or a serum-derived human monoclonal antibody (**sHIgM22**) resulted in approximately a twofold increase in remyelinating axons when compared to animals treated with saline or with antibodies that do not promote repair. Both pHIgM and **sHIgM22** show strong binding to CNS white matter and oligodendrocytes, while antibodies that did not accelerate remyelination do not. This differential staining pattern suggests that enhanced remyelination may result from direct stimulation of oligodendrocyte remyelination by binding to surface receptors on oligodendrocytes or glial progenitor cells. We propose the use of human polyclonal IgM or specific human monoclonal IgM antibodies as potential therapies to enhance myelin repair following CNS injury and disease. Copyright 2002 Wiley-Liss, Inc.

2/AB/3 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0004486714 BIOSIS NO.: 198529015613
LYM-22 WHICH DEFINES T SUPPRESSORS IS PRESENT ON T HELPER PRECURSORS
AUTHOR: CHAN M (Reprint); TADA N; HAMMERLING U; STUTMAN O
AUTHOR ADDRESS: MEMORIAL SLOAN-KETTERING CANCER CENTER, NEW YORK, NY 10021,

USA**USA
JOURNAL: Federation Proceedings 44 (3): p788 1985
CONFERENCE/MEETING: 69TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, ANAHEIM, CALIF., USA, APR. 21-26, 1985.
FED PROC.
ISSN: 0014-9446
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

2/AB/4 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

12631853 EMBASE No: 2004228579
Neuron-binding human monoclonal antibodies support central nervous system neurite extension
Warrington A.E.; Bieber A.J.; Van Keulen V.; Ciric B.; Pease L.R.; Rodriguez M.
Dr. A.E. Warrington, Department of Neurology, Guggenheim 401, Mayo Clinic College of Medicine, 200 First St. SW, Rochester, MN 55905 United States

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Journal of Neuropathology and Experimental Neurology (J. NEUROPATHOL. EXP. NEUROL.) (United States) 2004, 63/5 (461-473)
CODEN: JNENA ISSN: 0022-3069
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 62

Two human IgMs (sHIgM12 and sHIgM42) were identified that supported in vitro central nervous system (CNS) neurite extension equal to the potent neurite stimulatory molecule laminin. Both IgMs bound to multiple cell types in unfixed CNS tissue and to the surface of neurons in culture. Both monoclonal antibodies (mAbs) overrode the inhibitory effect of CNS mouse myelin on granule cell neurite extension. Neither mAb bound to the surface of mature oligodendrocytes or strictly colocalized with myelin proteins. Sialidase treatment eliminated the neuronal surface binding of both mAbs, whereas blocking sphingolipid synthesis with Fumonisin B, or removing GP1-linked proteins with PIPLC did not. When used as substrates for mixed neuron/glia aggregates, sHIgM12 and sHIgM42 supported robust neurite extension while astrocytes remained in the aggregates. In contrast, laminin supported astrocyte migration and spreading. Human mAbs that support neurite extension are novel factors that may be of use in encouraging axon repair following injury while minimizing glial cell infiltration. Both human mAbs were isolated from individuals with monoclonal gammopathy. Each individual has carried high mAb titers in circulation for years without detriment. sHIgM12 and sHIgM42 are therefore unlikely to be systemically pathogenic.

2/AB/5 (Item 1 from file: 351)
DIALOG(R)File 351:Derwent WPI

016715686
WPI Acc No: 2005-039961/200504
XRAM Acc No: C05-013422
Composition for promoting CNS remyelination or for treating demyelinating

diseases comprises a recombinant human monoclonal antibody that promotes CNS remyelination
Patent Assignee: ACORDA THERAPEUTICS (ACOR-N); MAYO FOUND MEDICAL EDUCATION & RES (MAYO-N)
Inventor: BIEBER A J; CHOJNICKI E; GRUSKIN E A; RODRIGUEZ M; WARRINGTON A E
Number of Countries: 108 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 2004110355	A2	20041223	WO 2004US15436	A	20040517	200504	B

Priority Applications (No Type Date): US 2003471235 P 20030516
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 2004110355	A2	E	67	A61K-000/00	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
Designated States (Regional): AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

Abstract (Basic): WO 2004110355 A2
Abstract (Basic):
NOVELTY - A pharmaceutical composition comprises a human monoclonal antibody selected from mAb **sHIgM22 (LYM 22)**, sHIgM46 (LYM46), ebvHIgM MSI19D10, Cb2BG8, MSI10E10, their mixtures, monomers, active fragments, binding partners, and recombinant antibodies derived from them, and a pharmaceutical carrier, vehicle or diluent.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) stimulating remyelination of central nervous system (CNS) axons in a mammal; and
(2) treating or preventing a demyelinating disease of the CNS in a mammal.
ACTIVITY - CNS-Gen. No biological data given.
MECHANISM OF ACTION - Gene therapy.
USE - The composition and methods are useful for promoting CNS remyelination or for treating demyelinating diseases as well as other CNS diseases that are of viral, bacterial or idiopathic origin, including neural dysfunction caused by spinal cord injury.
pp; 67 DwgNo 0/6

2/AB/6 (Item 2 from file: 351)
DIALOG(R)File 351:Derwent WPI

015961378
WPI Acc No: 2004-119219/200412
Related WPI Acc No: 1995-393077; 2003-238294
XRAM Acc No: C04-047932
XRPX Acc No: N04-095235
New human immunoglobulin M antibody for treating or preventing a demyelinating disease of the central nervous system in a human or domestic animal, such as multiple sclerosis
Patent Assignee: MAYO FOUND (MAYO-N)
Inventor: MILLER D J; PEASE L R; RODRIGUEZ M
Number of Countries: 001 Number of Patents: 001

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
US 20030185827	A1	20031002	US 94236520	A	19940429	200412 B
			US 96692084	A	19960808	
			US 97779784	A	19970107	
			US 99322862	A	19990528	
			US 2000580787	A	20000530	
			US 2000730473	A	20001205	
			US 200110729	A	20011113	

Priority Applications (No Type Date): US 200110729 A 20011113; US 94236520 A 19940429; US 96692084 A 19960808; US 97779784 A 19970107; US 99322862 A 19990528; US 2000580787 A 20000530; US 2000730473 A 20001205

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 20030185827	A1		159	A61K-039/395	CIP of application US 94236520 Cont of application US 96692084 CIP of application US 97779784 CIP of application US 99322862 CIP of application US 2000580787 CIP of application US 2000730473 CIP of patent US 5591629

Abstract (Basic): US 20030185827 A1

Abstract (Basic):

NOVELTY - An antibody (I) produced by injecting an immunocompetent host with an antibody peptide, and harvesting the antibody, where the peptide comprises a sequence (S1) of 113, 110, 124, or 133 amino acids, given in the specification, or active fragments, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) stimulating remyelination of central nervous system (CNS) axons in a mammal comprising administering a monoclonal antibody, or mixtures, monomers, active fragments, or recombinant antibodies derived from it, characterized by their ability to bind structures and cells within the CNS, including oligodendrocytes;

(2) stimulating the proliferation of glial cells in CNS axons in a mammal comprising administering a monoclonal antibody, or mixtures, monomers, active fragments, or recombinant antibodies derived from it, characterized by their ability to bind structures and cells within the CNS;

(3) treating or preventing a demyelinating disease of the CNS in a mammal comprising administering a monoclonal antibody, or mixtures, monomers, active fragments, or recombinant antibodies derived from it, characterized by their ability to bind structures and cells within the CNS, and to stimulate remyelination of axons of the CNS;

(4) stimulating, in vitro, the proliferation of glial cells from mixed cell culture comprising:

(a) culturing a mixed cell culture containing glial cells to proliferate cells;

(b) introducing into the mixed culture, a monoclonal antibody, or mixtures, monomers, active fragments, or recombinant antibodies derived from it, characterized by their ability to bind structures and cells within the CNS, including oligodendrocytes, to produce a monoclonal-treated mixed culture;

(c) maintaining the culture of (b) to allow proliferation of the cells; and

(d) harvesting the glial cells from the mixed culture;

(5) stimulating remyelination of CNS axons in a mammal comprising:

(a) culturing glial cells;

(b) introducing into the cell culture, a monoclonal antibody

capable of stimulating the cells to exhibit a calcium (Ca2+) peak, or mixtures, monomers, active fragments, or recombinant antibodies derived from it, the autoantibodies characterized by their ability to bind structures and cells within the CNS, including oligodendrocytes, to produce a treated glial cell culture;

(c) maintaining the cell culture of (b) for proliferation of treated cellsd) harvesting the treated cells from the culture to obtain glial cells; and

(e) introducing the glial cells of (d) into the CNS of the mammal;

(6) a DNA sequence or degenerate variant of it, which encodes an antibody, or a peptide analog, hapten, or active fragment of it, where the DNA sequence consists of:

(i) a sequence encoding a protein having S1; or

(ii) a sequence that hybridizes to (i);

(7) a recombinant DNA molecule comprising (6);

(8) a probe capable of screening for the antibody, peptide analog, hapten, or active fragment, in alternate species, prepared from (6);

(9) a unicellular host transformed with (7);

(10) an assay for screening drugs and other agents for the ability to modulate the production or mimic the activities of mAB **sHIgM22** , sHIgM46, or combinations of them, comprising:

(a) culturing an observable cellular test colony inoculated with a drug or agent;

(b) harvesting a supernatant from the colony; and

(c) examining the supernatant for the presence of the mAb, where an increase or decrease indicates the ability of the drug to modulate the activity of the mAb, where the mAb can induce remyelination, bind to neural tissue, promote Ca2+ signaling with oligodendrocytes, and promote cellular proliferation of glial cells;

(11) a test kit for demonstrating the presence of **sHIgM22**, sHIgM46, or combinations comprising the antibody, a specific binding partner of the antibody, other reagents, and directions for use of the kit, where the antibody or specific binding partner are detectably labeled;

(12) a recombinant virus transformed with (7);

(13) a vector comprising (714) a host vector system for the production of a polypeptide which comprises (13) in a host cell;

(15) obtaining a purified polypeptide comprising:

(a) introducing (13) into a host cell;

(b) culturing the cell to produce the polypeptide;

(c) recovering the polypeptide; and

(d) purifying the polypeptide;

(16) imaging a portion of the CNS comprising administering (I), labeled with a detectable label or imaging agent; and

(17) diagnosing or monitoring demyelination and/or remyelination of the CNS comprising using (16).

ACTIVITY - Nootropic; Neuroprotective; Antiviral; Antibacterial; Vulnerary. No suitable biological data is given.

MECHANISM OF ACTION - Cell therapy; Vaccine; Gene therapy.

USE - (I) Is used to stimulate remyelination of CNS axons, and to stimulate the proliferation of glial cells in CNS axons, optionally in vitro. (I) Is used to treat or prevent a demyelinating disease of the CNS in a human or domestic animal, such as multiple sclerosis, or a disease, other injury or dysfunction of the CNS, preferably the mammal is a mouse infected with Strain DA of Theiler's murine encephalomyelitis virus. (I) Is used to treat a spinal cord injury. (I) Is also used to screen drugs and other agents for the ability to modulate the production or mimic the activities of (I). (I) Can be used to image a portion of the CNS which can be used to diagnose or monitor demyelination and/or remyelination of the CNS (all claimed).

pp; 159 DwgNo 0/86

2/AB/7 (Item 3 from file: 351)
DIALOG(R)File 351:Derwent WPI

014245896
WPI Acc No: 2002-066596/200209
XRAM Acc No: C02-019870
XRPX Acc No: N02-049432
Novel neuromodulatory agent (a human IgM monoclonal antibody), promoting neurite outgrowth, regeneration, remyelination and neuroprotection in central nervous system, useful to treat post-infectious encephalomyelitis
Patent Assignee: MAYO FOUND MEDICAL EDUCATION RES (MAYO-N); MAYO FOUND MEDICAL EDUCATION & RES (MAYO-N)
Inventor: MILLER D J; PEASE L R; RODRIGUEZ M
Number of Countries: 094 Number of Patents: 006
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200185797	A1	20011115	WO 2000US14902	A	20000530	200209	B
AU 200061978	A	20011120	AU 200061978	A	20000530	200219	
EP 1294770	A1	20030326	EP 2000948498	A	20000530	200323	
			WO 2000US14902	A	20000530		
BR 200015875	A	20030624	BR 200015875	A	20000530	200343	
			WO 2000US14902	A	20000530		
JP 2004516807	W	20040610	WO 2000US14902	A	20000530	200438	
			JP 2001582396	A	20000530		
MX 2002011163	A1	20040901	WO 2000US14902	A	20000530	200553	
			MX 200211163	A	20021111		

Priority Applications (No Type Date): US 2000568351 A 20000510
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200185797	A1	E	219	C07K-016/06	
Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW				
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
AU 200061978	A				Based on patent WO 200185797
EP 1294770	A1	E		C07K-016/06	Based on patent WO 200185797
Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
BR 200015875	A			C07K-016/06	Based on patent WO 200185797
JP 2004516807	W		327	C12N-015/09	Based on patent WO 200185797
MX 2002011163	A1			A61K-039/395	Based on patent WO 200185797

Abstract (Basic): WO 200185797 A1
Abstract (Basic):

NOVELTY - Neuromodulatory agent (I) capable of promoting neurite outgrowth, regeneration, remyelination and neuroprotection in central nervous system (CNS), is new. (I) is human antibody, peptide analog, or hapten. (I) is capable of inducing remyelination, promoting cellular proliferation of glial cells, and promoting calcium ions signaling with oligodendrocytes.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a human or humanized antibody (II) to (I);

(2) an immortal cell line that produces (II);

(3) a DNA sequence or its degenerate variant (III) which encodes an antibody **sHIgM22 (LYM 22)**, ebvHigM MsI19D10, ebv HIgM CB2bG8, AKJR4, CB2iE12, CB2iE7 or MSI19E5, or its peptide analog, a hapten corresponding to antibody, or an active fragment of antibody, having one of 14 11 100-200 nucleotide sequences, all fully defined in the specifications;

(4) a recombinant DNA molecule (IV) comprising (III);

(5) a probe (V) capable of screening for the antibody or its peptide analog, hapten corresponding to antibody, or active fragment of antibody, in alternate species prepared from (III);

(6) a unicellular host (VI) transformed with (IV), where the DNA sequence is operatively linked to an expression control sequence;

(7) detecting (M1) presence or activity of (I), comprising:

(a) contacting a biological sample from a mammal with a binding partner of the neuromodulatory agent; and

(b) detecting if binding has occurred between the neuromodulatory agent from the sample and the binding partner;

(8) detecting the binding sites for (I), comprising:

(a) placing a neuromodulatory agent sample in contact with biological sample from a mammal; and

(b) examining the biological sample in binding studies for the presence of the labeled neuromodulatory agent, where the presence of the label neuromodulatory agent indicates a binding site for a neuromodulatory agent;

(9) testing the ability of a drug to modulate the activity of a neuromodulatory agent, comprisinga) culturing a colony of test cells which has a receptor for the neuromodulatory agent in a growth medium containing the neuromodulatory agent;

(b) adding the drug under test; and

(c) measuring the reactivity of the neuromodulatory agent with the receptor on the colony of test cells;

(10) an assay system for screening drugs for ability to modulate neuromodulatory agent production, or activity, comprising:

(a) culturing an observable cellular test colony inoculated with a drug or agent;

(b) harvesting a supernatant from the colony; and

(c) examining the supernatant for the presence of the neuromodulatory agent, where an increase or a decrease in the level of the neuromodulatory agent indicates a modulator;

(11) a test kit (K1) for the demonstration of a neuromodulatory agent in a eukaryotic cellular sample, comprises a detectably labeled specific binding partner of a neuromodulatory agent;

(12) a test kit (K2) for demonstrating the presence of a neuromodulatory agent in a eukaryotic cellular sample comprises a neuromodulatory agent, a specific binding partner of the neuromodulatory agent, other reagents, and directions for use;

(13) preventing and/or treating (M2) cellular debilitations, derangements and/or dysfunctions and/or other disease states in mammals including humans, and including such conditions in the CNS, comprising administering (I), or a modulator of the neuromodulatory agent;

(14) an antibody (VIII) produced by injecting (I) into a host;

(15) a recombinant virus transformed with (IV) or its derivative or fragment;

(16) an isolated nucleic acid (IX) comprising (III);

(17) an isolated nucleic acid (X) comprising (IX) operatively linked to a promoter of RNA transcription;

(18) a vector (XI) which comprises (X);

(19) a cell line (XIII) comprising (IX); and

(20) a vaccine (XVI) comprising (XI) and a carrier.

ACTIVITY - Antiparkinsonian; Neuroprotective; Nootropic; Virucide; Vulnerary.

Animals with chronic demyelination induced by Strain DA of Theiler's murine encephalomyelitis (TMEV) received intraperitoneal (IP) injections of purified antibodies in phosphate buffered saline. For TMEV infected animals the injection schedule consists of twice weekly injections of 50 micro-g in 100 ml. The duration of antibody treatment is five weeks. Animals are then sacrificed and spinal cord tissue is processed for morphological. For each different antibody treatment, nine chronically infected, female SJL/J mice were infected with antibody. At the end of the treatment period, six of the animals were perfused and processed for morphometric quantitation of demyelination/remyelination and three were sacrificed for frozen tissue that is used for assessment of axonal integrity. The human monoclonal antibodies **sHIgM 22**, sHIgM46 and ebvHIgM MS119D10 significantly promoted remyelination over other tested human monoclonal IgMs. There are no differences in the areas of myelin pathology between the treatment groups.

MECHANISM OF ACTION - Promotion, stimulation, regeneration and/or remyelination of neurons in central nervous system;

USE - (I) is useful for stimulating remyelination of CNS axons, stimulating proliferation of glial cells in CNS axons, or treating demyelinating disease of CNS in a mammal in need of such therapy. (I) is capable of binding to structures and cells within CNS. (I) is preferably useful for treating a demyelinating disease of central nervous system of a mouse infected with Strain DA of Theiler's murine encephalomyelitis (TMEV) or for treating a human being having multiple sclerosis, or a human or domestic animal with a viral demyelinating disease, or a post-neural disease of CNS. (I) is also useful for an in vitro method of stimulating the proliferation of glial cells from mixed cell culture. (I) is also useful for stimulating remyelination of central nervous system axons in a mammal. (II) is useful for preventing infection by a bacterium, virus or like pathogen that causes demyelination or other neurodegenerative condition in a subject. (XI) is useful for obtaining a polypeptide in purified form by recombinant techniques. (XV) is useful for inducing an immune response in a subject which has been exposed to or infected with a bacterium, a virus, or like pathogen that causes demyelination or other neurodegenerative condition. (XVI) is useful for treating a subject infected with or exposed by a bacterium, virus or like pathogen that causes demyelination or other neurodegenerative condition. (M2) is useful for treating multiple sclerosis, Parkinson's disease, Alzheimer's disease, amyotrophic lateral sclerosis (ALS), a viral demyelinating disease, a disease of the central nervous system, and other conditions in the central nervous system where nerves are damaged as by trauma. (All claimed).

ADVANTAGE - The monoclonal antibodies provide greater affinity for neural tissue and both diagnostic and therapeutic capabilitypp; 219 DwgNo 0/44

2/AB/8 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0357482 DBR Accession No.: 2005-03186 PATENT
Composition for promoting CNS remyelination or for treating demyelinating diseases comprises a recombinant human monoclonal antibody that promotes CNS remyelination - for central nervous system remyelination, virius and bacterium infection and spinal cord injury prevention,

therapy and gene therapy
AUTHOR: GRUSKIN E A; CHOJNICKI E; WARRINGTON A E; BIEBER A J; RODRIGUEZ M
PATENT ASSIGNEE: MAYO FOUND MEDICAL EDUCATION and RES; ACORDA THERAPEUTICS 2004
PATENT NUMBER: WO 2004110355 PATENT DATE: 20041223 WPI ACCESSION NO.: 2005-039961 (200504)
PRIORITY APPLIC. NO.: US 471235 APPLIC. DATE: 20030516
NATIONAL APPLIC. NO.: WO 2004US15436 APPLIC. DATE: 20040517
LANGUAGE: English
ABSTRACT: DERWENT ABSTRACT: NOVELTY - A pharmaceutical composition comprises a human monoclonal antibody selected from mAb **sHIgM22** (**LYM 22**), sHIgM46 (LYM46), ebvHIgM MSI19D10, Cb2BG8, MSI10E10, their mixtures, monomers, active fragments, binding partners, and recombinant antibodies derived from them, and a pharmaceutical carrier, vehicle or diluent. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) stimulating remyelination of central nervous system (CNS) axons in a mammal; and (2) treating or preventing a demyelinating disease of the CNS in a mammal. BIOTECHNOLOGY - Preferred Composition: The human recombinant antibody corresponds to or is derived from mAb **SHIgM22** (**LYM22**) or mAb SHIgM46 (LYM46). The composition further includes up to about 1-2 mg of a steroid, the steroid comprising or corresponding to methylprednisolone.Preferred Methods: Stimulating remyelination of CNS axons in a mammal comprises administering to the mammal the above composition or an amount of the monoclonal antibody, or its mixtures, monomers, active fragments, or derived recombinant antibodies having the ability to bind structures and cells within the CNS, including oligodendrocytes. Treating or preventing a demyelinating disease of the CNS in a mammal comprises administering to the mammal the above composition or an amount of the monoclonal antibody, or its mixtures, monomers, active fragments, or derived recombinant antibodies having the ability to bind structures and cells within the CNS, including oligodendrocytes, and to stimulate remyelination of axons of the CNS. The mammal is a human being having multiple sclerosis, or a human of domestic animal with a demyelinating disease, or a disease or other injury or dysfunction of the CNS. ACTIVITY - CNS-Gen. No biological data given. MECHANISM OF ACTION - Gene therapy. USE - The composition and methods are useful for promoting CNS remyelination or for treating demyelinating diseases as well as other CNS diseases that are of viral, bacterial or idiopathic origin, including neural dysfunction caused by spinal cord injury. ADMINISTRATION - The composition is given at a dose of about 500 ng-600 mug, or about 1.25-2.5 mug/kg. Administration can be intravenous, intraperitoneal, intrathecal, subcutaneous, sublingual, intramuscular, rectal, respiratory, or nasopharyngeal delivery (all claimed). EXAMPLE - No relevant example given. (67 pages)

2/AB/9 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0337620 DBR Accession Number: 2004-09912 PATENT
New human immunoglobulin M antibody for treating or preventing a demyelinating disease of the central nervous system in a human or domestic animal, such as multiple sclerosis - antibody production via cell culture for use in disease therapy
AUTHOR: RODRIGUEZ M; MILLER D J; PEASE L R
PATENT ASSIGNEE: MAYO FOUND 2003
PATENT NUMBER: US 20030185827 PATENT DATE: 20031002 WPI ACCESSION NO.:

2004-119219 (200412)
PRIORITY APPLIC. NO.: US 10729 APPLIC. DATE: 20011113
NATIONAL APPLIC. NO.: US 10729 APPLIC. DATE: 20011113
LANGUAGE: English
ABSTRACT: DERWENT ABSTRACT: NOVELTY - An antibody (I) produced by injecting an immunocompetent host with an antibody peptide, and harvesting the antibody, where the peptide comprises a sequence (S1) of 113, 110, 124, or 133 amino acids, given in the specification, or active fragments, is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) stimulating remyelination of central nervous system (CNS) axons in a mammal comprising administering a monoclonal antibody, or mixtures, monomers, active fragments, or recombinant antibodies derived from it, characterized by their ability to bind structures and cells within the CNS, including oligodendrocytes; (2) stimulating the proliferation of glial cells in CNS axons in a mammal comprising administering a monoclonal antibody, or mixtures, monomers, active fragments, or recombinant antibodies derived from it, characterized by their ability to bind structures and cells within the CNS; (3) treating or preventing a demyelinating disease of the CNS in a mammal comprising administering a monoclonal antibody, or mixtures, monomers, active fragments, or recombinant antibodies derived from it, characterized by their ability to bind structures and cells within the CNS, and to stimulate remyelination of axons of the CNS; (4) stimulating, in vitro, the proliferation of glial cells from mixed cell culture comprising: (a) culturing a mixed cell culture containing glial cells to proliferate cells; (b) introducing into the mixed culture, a monoclonal antibody, or mixtures, monomers, active fragments, or recombinant antibodies derived from it, characterized by their ability to bind structures and cells within the CNS, including oligodendrocytes, to produce a monoclonal-treated mixed culture; (c) maintaining the culture of (b) to allow proliferation of the cells; and (d) harvesting the glial cells from the mixed culture; (5) stimulating remyelination of CNS axons in a mammal comprising: (a) culturing glial cells; (b) introducing into the cell culture, a monoclonal antibody capable of stimulating the cells to exhibit a calcium (Ca2+) peak, or mixtures, monomers, active fragments, or recombinant antibodies derived from it, the autoantibodies characterized by their ability to bind structures and cells within the CNS, including oligodendrocytes, to produce a treated glial cell culture; (c) maintaining the cell culture of (b) for proliferation of treated cells; (d) harvesting the treated cells from the culture to obtain glial cells; and (e) introducing the glial cells of (d) into the CNS of the mammal; (6) a DNA sequence or degenerate variant of it, which encodes an antibody, or a peptide analog, hapten, or active fragment of it, where the DNA sequence consists of: (i) a sequence encoding a protein having S1; or (ii) a sequence that hybridizes to (i); (7) a recombinant DNA molecule comprising (6); (8) a probe capable of screening for the antibody, peptide analog, hapten, or active fragment, in alternate species, prepared from (6); (9) a unicellular host transformed with (7); (10) an assay for screening drugs and other agents for the ability to modulate the production or mimic the activities of mAB **sHIgM22**, sHIgM46, or combinations of them, comprising: (a) culturing an observable cellular test colony inoculated with a drug or agent; (b) harvesting a supernatant from the colony; and (c) examining the supernatant for the presence of the mAb, where an increase or decrease indicates the ability of the drug to modulate the activity of the mAb, where the mAb can induce remyelination, bind to neural tissue, promote Ca2+ signaling with oligodendrocytes, and promote cellular proliferation of glial cells; (11) a test kit for demonstrating the presence of **sHIgM22**, sHIgM46, or combinations comprising the antibody, a specific binding

partner of the antibody, other reagents, and directions for use of the kit, where the antibody or specific binding partner are detectably labeled; (12) a recombinant virus transformed with (7); (13) a vector comprising (7); (14) a host vector system for the production of a polypeptide which comprises (13) in a host cell; (15) obtaining a purified polypeptide comprising: (a) introducing (13) into a host cell; (b) culturing the cell to produce the polypeptide; (c) recovering the polypeptide; and (d) purifying the polypeptide; (16) imaging a portion of the CNS comprising administering (I), labeled with a detectable label or imaging agent; and (17) diagnosing or monitoring demyelination and/or remyelination of the CNS comprising using (16). BIOTECHNOLOGY - Preferred Antibody: (I) Is monoclonal, polyclonal, or chimeric (bispecific). In (1), (2) and (3), the monoclonal antibody is of the immunoglobulin (Ig)M subtype. In (1) - (5), it is a human antibody and is mAb **sHIgM22** (**LYM 22**), sHIgM46 (LYM46) (both preferred), ebvHIgM MSI19D10, ebvHIgM CB2b-G8, MSI10E10, or mixtures, monomers, active fragments, binding partners or recombinant antibodies of them. The light and heavy chains of **SHIgM22** (**LYM22**) have sequences of 110 and 113 amino acids, respectively. The light and heavy chains of sHIgM46 (LYM46) have sequences of 133 and 124 amino acids, respectively. The monoclonal antibody has a sequence which corresponds to S1 or active fragments. In (4), the mixed culture is obtained from rat optic nerve or rat brain. Preferred Nucleic Acid: In (7), the DNA sequence is operatively linked to an expression control sequence which is selected from the early or late promoters of simian virus (SV40) or adenovirus, the lac, trp, TAC, or TRC system, the major operator and promoter regions of phage lambda, the control regions of fd coat protein, the promoter for 3-phosphoglycerate kinase, the promoters of acid phosphatase, or the promoters of the yeast alpha-mating factors. Preferred Host: The host is an Escherichia coli, Pseudomonas, Bacillus, Streptomyces, a yeast, Chinese Hamster Ovary, R1.1, B-W, L-M, COS 1, COS 7, BSC1, BSC40, or BMT10 cell, or is a plant, insect, or human cell in tissue culture. ACTIVITY - Nootropic; Neuroprotective; Antiviral; Antibacterial; Vulnerary. No suitable biological data is given. MECHANISM OF ACTION - Cell therapy; Vaccine; Gene therapy. USE - (I) Is used to stimulate remyelination of CNS axons, and to stimulate the proliferation of glial cells in CNS axons, optionally in vitro. (I) Is used to treat or prevent a demyelinating disease of the CNS in a human or domestic animal, such as multiple sclerosis, or a disease, other injury or dysfunction of the CNS, preferably the mammal is a mouse infected with Strain DA of Theiler's murine encephalomyelitis virus. (I) Is used to treat a spinal cord injury. (I) Is also used to screen drugs and other agents for the ability to modulate the production or mimic the activities of (I). (I) Can be used to image a portion of the CNS which can be used to diagnose or monitor demyelination and/or remyelination of the CNS (all claimed). ADMINISTRATION - Administration is by intravenous, intraperitoneal, intrathecal, subcutaneous, sublingual, intramuscular, rectal, respiratory or nasopharyngeal routes. Dose of monoclonal antibody is 0.5 - 400 mg/kg. IgM is administered at a dose of 0.5 - 2 g/kg (all claimed). EXAMPLE - No suitable example is given.(159 pages)

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